

b.) Remarks

Claim 1, 80 and 81 have been amended in order to recite the present invention with the specificity required by statute and claims 22, 56, 57 and 76-79 are cancelled in order to reduce the issues. No new matter has been added.

Claims 1, 14, 15, 18-24, 26, 27, 72, 74-75, 80 and 82-87 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification. The Examiner states he cannot find literal or figurative support for "differentiation of embryonic stem cell into a nervous system cell before determining of dorso-ventral axis." In response, this phrase has been deleted above.

Additionally, the Examiner contends the conditions (without retinoic acid or BMP-4) are inconsistent with the teachings of the specification. In response, by way of clarification, claims 80 and 81 are amended to recite that embryonic stem cells were cultured in the presence of stroma cells recognized by a monoclonal antibody produced by FERM BP-7573 and in the absence of retinoic acid or BMP-4. As taught in the specification, these embryonic stem cells were differentiated into dopaminergic neurons and nestin-positive neural stem cells (see Example 1 at specification, page 93, lines 7-8; page 94, lines 10-15; Fig. 4), nerve cells (see Example 4 at page 98, line 20 to page 99, line 3; page 99, lines 12-19), nervous ectodermal cells (see Example 7 at page 104, lines 12-21; page 105, lines 1-5), and nerve cells (see Example 9 at page 106, lines 30 to page 107, line 16). Also, in Example 14, as a result that embryonic stem cells were cultured in the presence of the stroma cells and in the absence of retinoic acid or BMP-4, and then BMP-4 was added during the culturing as recited in amended claim 1, the embryonic stem cells were differentiated into a neural crest or a neural tube.

In this regard, when embryonic stem cells are cultured in the presence of stroma cells as in amended claim 1, differentiation into nestin-positive neural stem cells can be induced. Differentiation into a neural tube or a neural crest can then be induced by adding BMP-4 to the medium with further culturing.

Claims 1, 14, 15, 18-24, 26, 27, 56, 57, 72, 74-75 and 80-87 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the present invention. In this regard, the Examiner states there are no conditions set forth for preculturing, and the step including BMP-4 appears to pertain more closely to forming cells of neural lineage. In response, "pre-culturing" is replaced with --culturing-- (see specification page 40, lines 20-27; page 41, lines 18-21 and 26-35).

Claim 81 is rejected under 35 U.S.C. §102(b) as being anticipated by Thomson et al. (*Biol. Reprod.* 1996 Aug; 55(2):254-9) for the reasons discussed at pages 8 and 9 of the Office Action. This rejection is respectfully traversed.

Claim 81 relates to a method for producing a nestin-positive neural stem cell by culturing an embryonic stem cell in the absence of both retinoic acid and BMP-4 and in the presence of a stroma cell which is recognized by a monoclonal antibody produced by hybridoma FERM BP-7573. Thomson discloses use of mouse embryonic fibroblast cells as feeder cells, but neither discloses nor suggests use of the stroma cell described in amended claim 81.

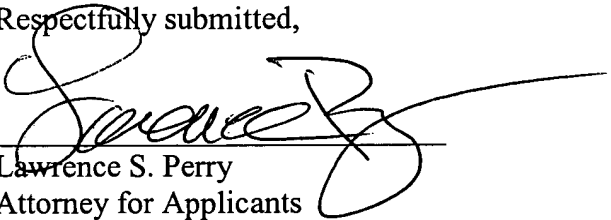
In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition.

Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 1, 15, 18-21, 23, 24, 72, 74, 75 and 80-87 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Lawrence S. Perry', is written over a horizontal line.

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